

**What is Claimed is:**

1. A method of identifying a culture medium component, comprising the steps of:

measuring first indicia of a property of a plurality of first culture media which each contains a respective first test compound from within a first test library;

determining a relationship between at least one parameter of the first test compounds and the measured first indicia of the property of the plurality of first culture media;

determining a test requirement relating to the measured first indicia; and

identifying a second test library containing a plurality of second test compounds as components of a plurality of second culture media which based on the relationship are expected to provide second indicia of the property which meets the test requirement.

2. The method of Claim 1, wherein the plurality of first test compounds is selected from the first test library using a space-filling technique; and wherein the plurality of second test compounds is selected from the second test library using a space-filling technique.

3. The method of Claim 1, wherein said step of determining a relationship comprises the step of determining  $\hat{y}_i = f(x_{ij})$ , where  $x_{ij}$  denotes a parameter,  $i$  ranges from 1 to  $n$  where  $n$  represents the number of first culture media in the plurality thereof,  $j$  ranges from 1 to  $d$  where  $d$  represents the number of parameters, and  $\hat{y}_i$  represents an estimate of the measured first indicia of the property of the plurality of first culture media.

4. The method of Claim 3, wherein said step of determining a test requirement comprises the step of determining a range of acceptable indicia of the property.

5. The method of Claim 4, wherein said identifying step comprises determining from  $\hat{y}_i = f(x_{ij})$  estimated indicia of the property of a plurality of

second culture media which each contains a respective test compound; and wherein at least one of the second culture media contains a test compound that is not within the first test library.

6. The method of Claim 5, wherein said identifying step further comprises:

determining which of the estimated indicia are within the range of acceptable indicia; and

determining from the estimated indicia that are within the range, the plurality of second test compounds from the second test library.

7. The method of Claim 6, further comprising the step of measuring second indicia of the property of the plurality of second culture media.

8. The method of Claim 7, wherein  $f(x_{ij})$  is a non-parametric regression formula.

9. The method of Claim 3, wherein  $f(x_{ij})$  is a non-parametric regression formula.

10. The method of Claim 1, wherein said step of determining a relationship comprises the step of:

determining a distance function  $d(x_1, x_2)$  between a first value of a parameter,  $x_1$ , of a first test compound and a second value of the parameter,  $x_2$ , of a second test compound not within the plurality of first test compounds; and

estimating indicia of the property of a culture medium containing the second test compound as the indicia of the property of the culture medium containing the first test compound if  $d(x_1, x_2) \leq d_{\text{cutoff1}}$ , where  $d_{\text{cutoff1}}$  is a cutoff distance for the first test compound.

11. The method of Claim 1, wherein said measuring step is preceded by a step of defining a first test library by representing each of a plurality of groups of compound isomers from a compound space as a respective candidate compound.

12. The method of Claim 11, further comprising the step of expanding less than all of the candidate compounds determined in said representing step into their constituent compound isomers using a space-filling technique.

13. The method of Claim 1, wherein the at least one parameter is selected from the group consisting of whole molecule, sequence-specific, and topological parameters.

14. The method of Claim 1, wherein the at least one parameter is a whole molecule parameter.

15. The method of Claim 14, wherein the whole molecule parameter is selected from the group consisting of total charge, molecular weight, isoelectric point, total dipole moment, isotropic surface area, electronic charge index, and hydrophobicity.

16. A culture medium component identified by the method of Claim 1.

17. A culture medium comprising the culture medium component of Claim 16.

18. The method of Claim 1, wherein the first and second test libraries are selected from the group consisting of peptide, polynucleotide, nucleic acid, carbohydrate, free fatty acid, and lipid libraries.

19. The method of Claim 1, wherein the first and second test libraries are test peptide libraries.

20. The method of Claim 19, wherein the first and second test peptide libraries consist of peptides having a length in a range from about four amino acids to about twenty amino acids.

21. The method of Claim 19, wherein the peptides in the first test library comprise at least one amino acid position that is nonvariable or is designated by a limited number of possible amino acids.

22. The method of Claim 19, wherein the peptides in the second test library comprise at least one amino acid position that is nonvariable or is designated by a limited number of possible amino acids.

23. The method of Claim 1, wherein said step of measuring first indicia is preceded by the step of forming a plurality of cell cultures which each contains a respective first culture medium from within the plurality thereof.

24. The method of Claim 23 further comprising the step of conditioning the cell cultures to grow in both chemically-undefined and chemically-defined media prior to said measuring step.

25. The method of Claim 23, wherein the cell cultures are selected from the group consisting of mammalian, insect, plant, fungal, yeast, protozoan and bacterial cell cultures.

26. The method of Claim 23, wherein the plurality of culture media are chemically-defined culture media.

27. The method of Claim 23, wherein the measured property of the plurality of first culture media is the ability to alter the growth, proliferation, maturation or differentiation of cultured cells.

28. The method of Claim 23, wherein the measured property of the plurality of first culture media is the ability to alter peptide or protein production by cultured cells.

29. The method of Claim 28, wherein the peptide or protein is selected from the group consisting of antigens, toxins, antibodies, hormones, growth factors, cytokines, clotting factors, and enzymes.

30. The method of Claim 23, wherein the measured property of the plurality of first culture media is the ability to alter the production of a compound selected from the group consisting of antibiotics, steroids, carbohydrates lipids and nucleic acids by cultured cells.

31. A method of defining a test compound library, comprising the step of representing each of a plurality of groups of compound isomers from within a compound space as a respective candidate compound. GROUP-BUILD ALGORITHM

32. The method of Claim 31, wherein said representing step is followed by the steps of

selecting less than all of the candidate compounds using a space-filling technique; and

expanding the less than all of the candidate compounds determined in said selecting step into their constituent compound isomers.

33. The method of Claim 32, further comprising the step of selecting at least one constituent compound isomer for each of the candidate compounds.

34. The method of Claim 31, wherein the compound space and test compound library consist of compounds selected from the group consisting of peptides, polynucleotides, nucleic acids, carbohydrates, free fatty acids, and lipids.

35. The method of Claim 31, wherein the compound space is a peptide space and the test compound library is a test peptide library.

36. A test compound library wherein each of a plurality of compound isomers from within a compound space is represented as a respective candidate compound.

37. The test compound library of Claim 36, wherein the compound space is a peptide space and the test compound library is a test peptide library.

38. A test compound library formed by the method of Claim 31.

39. A test compound library formed by the method of Claim 32.

40. The test compound library of Claim 39, wherein the compound space is a peptide space and the test compound library is a test peptide library.

41. A method of identifying a culture medium component, comprising the steps of:

defining a first test library by representing each of a plurality of groups of compound isomers from within a compound space as a respective candidate compound;

measuring first indicia of a property of a plurality of first culture media which each contains a respective first test compound from within the first test library;

determining a relationship between at least one parameter of the first test compounds and the measured first indicia of the property of the plurality of first culture media;

determining a test requirement relating to the measured first indicia; and

identifying a plurality of second test compounds from within the compound space as components of a plurality of second culture media which based on the relationship are expected to provide second indicia of the property which meets the test requirement.

42. The method of Claim 41, wherein said defining step further comprises expanding the less than all of the candidate compounds determined in said representing step into their constituent compound isomers using a space-filling technique.

43. The method of Claim 42, wherein said defining step further comprises selecting at least one constituent compound isomer from each of the candidate compounds.

44. The method of Claim 41, wherein the plurality of first test compounds is selected from the first test library using a space-filling technique.

45. The method of Claim 41, wherein said step of determining a relationship comprises the step of determining  $\hat{y}_i = f(x_{ij})$ , where  $x_{ij}$  denotes a parameter,  $i$  ranges from 1 to  $n$  where  $n$  represents the number of first culture media in the plurality thereof,  $j$  ranges from 1 to  $d$  where  $d$  represents the number of parameters, and  $\hat{y}_i$  represents an estimate of the measured first indicia of the property of the plurality of first culture media.

46. The method of Claim 45, wherein said step of determining a test requirement comprises the step of determining a range of acceptable indicia of the property.

47. The method of Claim 46, wherein said identifying step comprises determining from  $\hat{y}_i = f(x_{ij})$  estimated indicia of the property of a plurality of second culture media which each contains a respective test compound, wherein at least one of the second culture media contains a test compound that is not within the first test library.

48. The method of Claim 47, wherein said identifying step further comprises:

determining which of the estimated indicia are within the range of acceptable indicia; and

determining from the estimated indicia that are within the range, the plurality of second test compounds from the compound space.

49. The method of Claim 45, wherein  $f(x_{ij})$  is a non-parametric regression formula.

50. The method of Claim 41, wherein said step of determining a relationship comprises the step of:

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determining a distance function  $d(x_1, x_2)$  between a first value of a parameter,  $x_1$ , of a first test compound and a second value of the parameter,  $x_2$ , of a second test compound not within the plurality of first test compounds; and estimating indicia of the property of a culture medium containing the second test compound as the indicia of the property of the culture medium containing the first test compound if  $d(x_1, x_2) \leq d_{\text{cutoff1}}$ , where  $d_{\text{cutoff1}}$  is a cutoff distance for the first test compound.

51. The method of Claim 41, wherein the at least one parameter is selected from the group consisting of whole molecule, sequence-specific, and topological parameters.

52. The method of Claim 41, wherein the at least one parameter is a whole molecule parameter.

53. The method of Claim 41, wherein the compound space is selected from the group consisting of peptide, polynucleotide, nucleic acid, carbohydrate, free fatty acid, and lipid spaces.

54. The method of Claim 41, wherein the compound space is a peptide space.

55. A culture medium component identified by the method of Claim 41.

56. A culture medium comprising the culture medium component of Claim 55.

57. The method of Claim 41, wherein said step of measuring first indicia of the property comprises adding each of the plurality of first culture media to a respective cell culture to form a plurality of cell cultures each containing a respective culture medium containing a respective first test compound.



58. The method of Claim 57, wherein the plurality of cell cultures is selected from the group consisting of mammalian, insect, plant, fungal, yeast, protozoan and bacterial cell cultures.

59. A method of predicting indicia of a property of a peptide, comprising the steps of:

measuring indicia of an activity of a plurality of test peptides from a test peptide library;

determining a relationship between the measured indicia of the activity and at least one whole molecule parameter of the plurality of test peptides;

predicting the indicia of the activity of a peptide not within the plurality of test peptides based on the relationship.

60. The method of Claim 59, wherein the first plurality of test peptides from the test peptide library is selected using a space-filling technique.

61. The method of Claim 59, wherein the at least one whole molecule parameter comprises a parameter selected from the group consisting of total charge, molecular weight, isoelectric point, total dipole moment, isotropic surface area, electronic charge index, and hydrophobicity.

62. The method of Claim 59, wherein at least two whole molecule parameters of the plurality of test peptides are selected from the group consisting of total charge, molecular weight, isoelectric point, total dipole moment, isotropic surface area, electronic charge index, and hydrophobicity.

63. The method of Claim 59, wherein the at least one whole molecule parameter comprises hydrophobicity, molecular weight, total dipole moment, and total charge.

64. The method of Claim 59, wherein the at least one whole molecule parameter comprises molecular weight and at least one additional parameter selected from the group consisting of total charge, isoelectric point, total dipole moment, isotropic surface area, electronic charge index, and hydrophobicity.



74. A method of identifying a peptide with a predicted indicia of an activity that satisfies a test requirement, comprising the steps of:

measuring first indicia of an activity of a plurality of first test peptides from a first test peptide library;

determining a relationship between the measured first indicia of the activity and at least one whole molecule parameter of the plurality of first test peptides;

determining a test requirement relating to the measured first indicia; and

identifying a second test peptide library containing a plurality of second test peptides which based on the relationship are expected to provide second indicia of the activity that meets the test requirement.

75. The method of Claim 74, wherein the plurality of first test peptides is selected from the first test peptide library using a space-filling technique.

76. The method of Claim 74, wherein said step of determining a relationship comprises the step of determining  $\hat{y}_i = f(x_{ij})$ , where  $x_{ij}$  denotes a parameter,  $i$  ranges from 1 to  $n$  where  $n$  represents the number of first test peptides in the plurality thereof,  $j$  ranges from 1 to  $d$  where  $d$  represents the number of whole molecule parameters, and  $\hat{y}_i$  represents an estimate of the measured first indicia of the activity of the plurality of first test peptides.

77. The method of Claim 76, wherein said step of determining a test requirement comprises the step of determining a range of acceptable indicia of the activity.

78. The method of Claim 77, wherein said identifying step further comprises:

determining which of the estimated indicia are within the range of acceptable indicia; and

determining from the estimated indicia that are within the range, the plurality of second test peptides from the second test peptide library.

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79. The method of Claim 76, wherein  $f(x_{ij})$  is a non-parametric regression formula.

80. The method of Claim 74, wherein said step of determining a relationship comprises the step of:

5 determining a distance function  $d(x_1, x_2)$  between a first value of a whole molecule parameter,  $x_1$ , of a first test peptide and a second value of the whole molecule parameter,  $x_2$ , of a second test peptide not within the first test peptide library; and

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estimating indicia of the activity of the second test peptide as the indicia of the activity of the first test peptide if  $d(x_1, x_2) \leq d_{\text{cutoff1}}$ , where  $d_{\text{cutoff1}}$  is a cutoff distance for the first test peptide.

81. The method of Claim 74, wherein said measuring step is preceded by the step of defining a first test peptide library by representing each of a plurality of groups of peptide isomers from a first peptide space as a respective candidate peptide.

82. The method of Claim 81, further comprising the step of expanding less than all of the candidate peptides determined in said representing step into their constituent compound peptides using a space-filling technique.

83. The method of Claim 74, wherein the at least one whole molecule parameter is selected from the group consisting of total charge, molecular weight, isoelectric point, total dipole moment, isotropic surface area, electronic charge index, and hydrophobicity.

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84. The method of Claim 74, wherein at least two whole molecule parameters are selected from the group consisting of total charge, molecular weight, isoelectric point, total dipole moment, isotropic surface area, electronic charge index, and hydrophobicity.

85. The method of Claim 74, wherein the at least one parameter comprise hydrophobicity, molecular weight, total dipole moment, and total charge.

86. The method of Claim 74, wherein the at least one whole molecule parameter is molecular weight and at least one additional parameter selected from the group consisting of total charge, isoelectric point, total dipole moment, isotropic surface area, electronic charge index, and hydrophobicity.

87. The method of Claim 74, wherein the activity is binding to a receptor.

88. The method of Claim 74, wherein the activity is enhancement or inducement of a biological activity in a cell.

89. The method of Claim 74, wherein the activity is inhibition or prevention of a biological activity in a cell.

90. The method of Claim 88 or Claim 89, wherein the cell is a cell cultured *in vitro*.

91. The method of Claim 90, wherein said step of measuring first indicia of the activity comprises:

forming a plurality of culture media that each contains a respective test peptide from the plurality thereof; and

adding each of the plurality of culture media to a respective cell culture to form a plurality of cell cultures each containing a respective culture medium containing a respective first test compound.

92. The method of Claim 74, wherein the activity is inhibition or prevention of activation of a receptor.

93. The method of Claim 74, wherein the activity is enhancement or inducement of activation of a receptor.

94. The method of Claim 74, wherein the test peptide library consists of peptides having a length in a range from about four amino acids to about twenty amino acids.

95. The method of Claim 74, wherein the test peptide library consists of peptides having a length in a range from about four amino acids to about ten amino acids.

96. A method of identifying a culture medium component, comprising the steps of:

culturing a plurality of first cell cultures in a plurality of first culture media each containing a respective first test compound from a first test library;

measuring first indicia of a property of the plurality of first culture media in the plurality of first cell cultures;

determining a relationship between the measured first indicia of the property and at least one parameter of the plurality of first culture media;

determining a test requirement relating to the measured first indicia; and culturing a plurality of second cell cultures in a plurality of second culture media each containing a respective second test compound from a second test library;

wherein based on the relationship the plurality of second culture media containing the second test compounds are predicted to give indicia of the property that satisfy the test requirement.

97. The method of Claim 96, further comprising the step of reformulating the culture medium containing the identified culture medium component to omit components.

98. The method of Claim 97, wherein at least one component is omitted from the culture medium formulation.

99. The method of Claim 96, wherein said step of culturing a plurality of first cell cultures further comprises the steps of:

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comparing the measured indicia of the property for the same test compound in the chemically-defined culture medium and the chemically-undefined culture medium.

101. The method of Claim 96, wherein the plurality of first and second culture media comprise a concentration of an undefined protein component in a range from about 0.1% (w/v) to about 2.5%(w/v).

103. The method of Claim 96, wherein the plurality of first and second culture media comprise a concentration of an undefined protein component in a range from about 0.25% (w/v) to about 1%(w/v).

104. The method of Claim 96, wherein the plurality of first and second culture media comprise a concentration of serum in a range from about 0.05% (v/v) to about 30%(v/v).

105. The method of Claim 96, wherein the plurality of first and second cell cultures is selected from the group consisting of mammalian, insect, plant, fungal, yeast, protozoan and bacterial cell cultures.

106. The method of Claim 96, wherein the plurality of first and second culture media are chemically-defined culture media.

107. The method of Claim 96, wherein the plurality of first and second culture media are liquid culture media.

108. The method of Claim 96, wherein the measured property of the plurality of first culture media is the ability to alter growth, maturation, proliferation, or differentiation of cultured cells.

109. The method of Claim 96, wherein the measured property of the plurality of first culture media is the ability to alter peptide or protein synthesis by cultured cells.

110. The method of Claim 109, wherein the peptide or protein is selected from the group consisting of antigens, toxins, antibodies, hormones, growth factors, cytokines, clotting factors, and enzymes.

111. The method of Claim 96, wherein the measured property of the plurality of first culture media is the ability to alter the synthesis of a compound selected from the group consisting of antibiotics, steroids, carbohydrates, lipids and nucleic acids by cultured cells.

112. The method of Claim 96, wherein the measured property of the plurality of first culture media is the ability to alter peptide or protein secretion by cultured cells.

113. A culture medium component identified by the method of Claim 96.

114. A culture medium comprising the culture medium component of Claim 113.

115. The culture medium of Claim 114, wherein the culture medium comprises a concentration of an undefined protein component in a range from about 0.1% (w/v) to about 2.5%(w/v).



116. The culture medium of Claim 115, wherein the undefined protein component is selected from the group consisting of hydrolysates, digests, extracts and infusions.

117. The culture medium of Claim 114, wherein the culture medium comprises a concentration of serum in a range from about 0.05% (v/v) to about 30%(v/v).

118. The culture medium of Claim 114, wherein the culture medium comprises insulin.

119. An apparatus for identifying a culture medium component, comprising:

means for determining a relationship between measured first indicia of a property of a plurality of first culture media which each contains a respective first test compound from within a first test library and at least one parameter of the first test compounds; and

means for identifying a second test library containing a plurality of second test compounds as components of a plurality of second culture media which based on the relationship are expected to provide second indicia of the property which meets a test requirement relating to the measured first indicia.

120. The apparatus of Claim 119, wherein said determining means comprises means for determining  $\hat{y}_i = f(x_{ij})$ , where  $x_{ij}$  denotes a parameter,  $i$  ranges from 1 to  $n$  where  $n$  represents the number of first culture media in the plurality thereof,  $j$  ranges from 1 to  $d$  where  $d$  represents the number of parameters, and  $\hat{y}_i$  represents an estimate of the measured first indicia of the property of the plurality of first culture media.

121. The apparatus of Claim 120, wherein said identifying means comprises means for determining from  $\hat{y}_i = f(x_{ij})$  estimated indicia of the property of a plurality of second culture media which each contains a respective test

5 compound, wherein at least one of the second culture media contains a test compound that is not within the first test library.

122. The apparatus of Claim 119, wherein said determining means comprises:

5 means for determining a distance function  $d(x_1, x_2)$  between a first value of a parameter,  $x_1$ , of a first test compound and a second value of a parameter,  $x_2$ , of a second test compound not within the plurality of first test compounds; and

10 means for estimating indicia of the property of a culture medium containing the second test compound as the indicia of the property of the culture medium containing the first test compound if  $d(x_1, x_2) \leq d_{\text{cutoff1}}$ , where  $d_{\text{cutoff1}}$  is a cutoff distance for the first test compound.

123. A computer program product readable by a machine and tangibly embodying a program of instructions executable by the machine to perform the method steps of:

5 determining a relationship between measured first indicia of a property of a plurality of first culture media which each contains a respective first test compound from within a first test library and at least one parameter of the first test compounds, and

10 identifying a second test library containing a plurality of second test compounds as components of a plurality of second culture media which based on the relationship are expected to provide second indicia of the property which meets a test requirement relating to the measured first indicia.

5 124. The computer program product of Claim 123, wherein said determining step further comprises determining  $\hat{y}_i = f(x_{ij})$ , where  $x_{ij}$  denotes a parameter,  $i$  ranges from 1 to  $n$  where  $n$  represents the number of first culture media from within a plurality thereof,  $j$  ranges from 1 to  $d$  where  $d$  represents the number of parameters, and  $\hat{y}_i$  represents an estimate of the measured first indicia of the property of the first test compounds.

